REMARKS

Claims 1 – 16, 19 – 21, 26 – 28, 32 – 36, 40, 43, 46, 47 53, 57 and 64 are currently pending in the present application. Claims 16, 19 – 21, 26 – 28, 35, 36, 40, 43, 46, 53, 57 and 64 are withdrawn. Claims 17 – 18, 22 – 25, 29 – 31, 37 – 39, 41 – 42, 44 – 45, 48 – 52, 54 – 56, 58 – 63 and 65 – 82 have been cancelled.

The informalities of the disclosure as pointed out by the Examiner have been corrected. Reconsideration and withdrawal of the objection thereto are respectfully requested.

The objection to claims 1 – 12, 32 – 34 and 47 and the indication that correction is not required at this time are duly noted.

Claim 32 has been amended to clarify that this claim is directed to a method involving repeating steps a and b of the method of claim 1 with a different protein or part protein than the one used in the first time steps a and b are performed so that the results may be compared. Accordingly, the claim is directed to a subset of the method of claim 1 and does not broaden claim 1. Reconsideration and withdrawal of the objection are therefore respectfully requested.

The rejection of claims 1 – 15 and 32 – 34 under 35 U.S.C. 112, second paragraph, as indefinite, is respectfully traversed.

For purposes of definiteness, the relevant question is whether one of skill in the art could understand the scope of the claim. The MPEP states that:

> In reviewing a claim for compliance with 35 U.S.C. 112, second paragraph, the examiner must consider the claim as a whole to determine whether the claim apprises one of ordinary skill in the art of its scope and, therefore, serves the notice function required by 35 U.S.C. 112, second paragraph, by providing clear warning to others as to what constitutes infringement of the patent. See, e.g., *Solomon v. Kimberly-Clark Corp.*, 216 F.3d 1372, 1379, 55 USPQ2d 1279, 1283 (Fed. Cir. 2000).

In the present case, that test is clearly met, because one of skill in the art would readily understand the steps required to practice the claimed method. As a result, one of skill in the art could readily determine whether or not some activity constitutes infringement of these claims.

The Office Action alleges claim 1 is indefinite as it is not clear that the method will necessarily result in the identification of pain-regulating substances. The Office Action adds that that the claims do not require that the proteins or part proteins encompassed therein have any particular functional activity. Thus, the rejection appears to be based on an assumption that the claimed method might not work to identify a pain-regulating substance. Even assuming, *arguendo*, that this were true, the scope of the claim is not rendered indefinite.

Nevertheless, supposing that the operability of the claimed method to achieve the desired end result is properly analyzed in accordance with the law related to indefiniteness, the claims are definite. This is because a person of skill in the art would expect that the claimed method to have a reasonable probability of success. The person of skill in the art would be aware of the various articles in the literature which show that members of the MAP-kinase family have relevance to nociception, i.e. the perception and transduction of pain. In particular, relevant articles show that certain spinal MAP-kinases are relevant to chronic neuropathic pain models. Summaries of certain of these articles are provided in Appendix A attached hereto.

These documents show the relevance of the p38MAPK/ERK-signal transduction pathway in the development of neuropathic pain. In view of this evidence that certain MAP-kinases are relevant to chronic neuropathic pain models, a person of skill in the art would have a reasonable expectation of success for the claimed methods of detecting a pain-regulating substance with PIM-kinases.

Further, the inventors of the present application have shown in an animal model (rat) that PIM-1-kinase knock-outs have a significantly slowed cold allodynia as displayed by the following graph. This graph displays data comparing cold

allodynia in PIM-1-kinase knock-out rats against rats where the protein has not been knocked out.

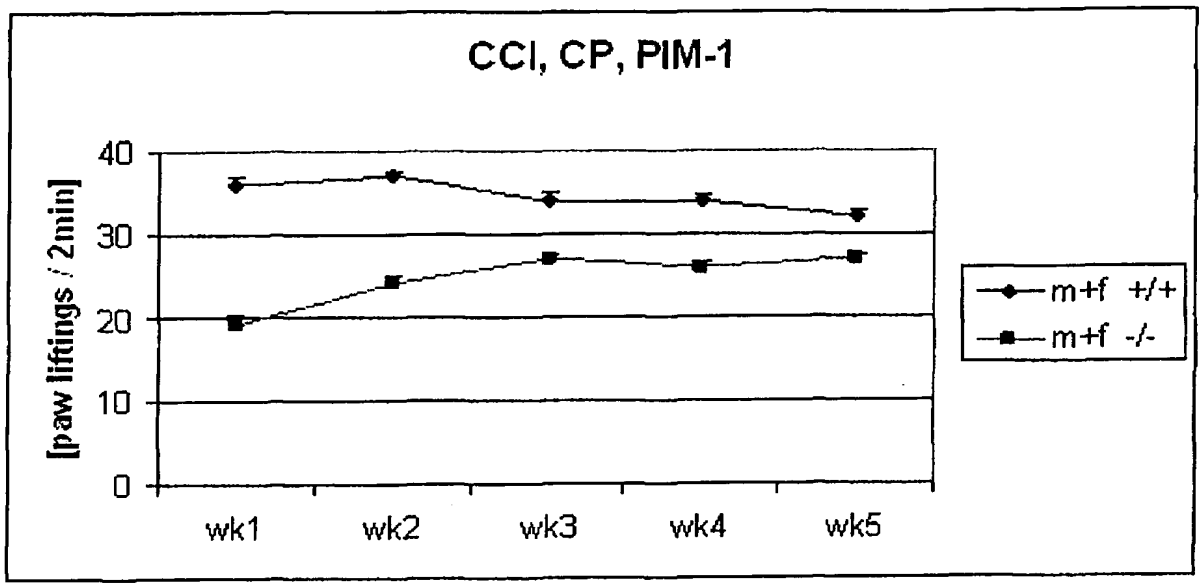


Figure 1

The results in Figure 1 show that PIM-1-kinase knock-out rats (the lower curve) have a significantly reduced response to pain. Therefore, PIM-1-kinase has relevance to neuropathic pain.

The same is true for the highly homologous PIM3-kinase. Attached as Appendix B to this Reply is a sequence alignment between human PIM3-sequence and the human PIM1-sequence.

In view of the foregoing, these claims are definite.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

The rejection of claim 7 as indefinite is respectfully traversed. Claim 7 is amended to clarify that it is the protein or part protein (of interest) which is

expressed. Reconsideration and withdrawal of this rejection are respectfully requested.

The rejection of claim 10 as indefinite is respectfully traversed. Claim 10 refers to measuring binding by displacement of a known labeled ligand or by the activity bound from a labeled test substance. Thus, the idea is that the labeled test substance has some activity which is detectable. By way of example, the specification provides for "radioactive, fluorescent, or luminescent labeling" (see paragraph [00135]. Thus, for instance, it is the radioactivity which might be detected. This is how a person of skill in the art would understand the claim and accordingly, the claim is believed to be in definite form. Reconsideration and withdrawal of this rejection are respectfully requested.

The rejection of claims 32-34 as indefinite is respectfully traversed. As indicated above, claim 32 is amended to clarify that the claim adds a repetition of steps a and b of the method of claim 1, using a different protein or part protein. The results obtained from the first performance of steps a and b are then compared with those from the second performance of steps a and b. Any difference in the results may then be attributed to the use of a different protein or part protein in the first and second performance. Claims 33 and 34 are amended to provide proper syntax and grammer to track the language of claim 32. As amended, these claims are definite and reconsideration and withdrawal of the rejections are respectfully requested.

The rejection of claims 1 – 15 and 32 – 34 as not being properly enabled is respectfully traversed. The enablement requirement is satisfied where the specification describes the claimed subject matter in such a way as to enable any person skilled in the art to which it pertains to make and/or use the invention. Thus, enablement is judged in view of the combined teachings of the specification and the knowledge of one skilled in the art.

As evidenced by the literature summarized in Appendix A, persons of skill in the art would be aware of the relevance members of the MAP-kinase family have to nociception. As discussed above, the articles show that certain spinal MAP-kinases are relevant to chronic neuropathic pain models. In particular, the documents show the relevance of the p38MAPK/ERK-signal transduction pathway in the development of neuropathic pain. As a result, and in view of this evidence that certain MAP-kinases are relevant to chronic neuropathic pain models, a person of skill in the art would have a reasonable expectation of success for the claimed methods of detecting a pain-regulating substance with PIM-kinases.

Further, the results provided in Figure 1 above show that PIM-1-kinase has relevance to neuropathic pain. Based on the homology of PIM-3-kinase to PIM-1-kinase, as shown in the sequence alignment between the human PIM3-sequence and the human PIM1-sequence (in Appendix B to this Reply), a person of skill in the art would reasonably expect that PIM-3-kinase has functional properties similar to if not largely the same as those of PIM-1-kinase.

Thus, persons of skill in the art would reasonably expect that the claimed methods of detecting pain-regulating substances with PIM-kinases would be operative.

The U.S. Court of Customs and Patent Appeals has stated that "The first paragraph of § 112 requires nothing more than objective enablement. How such a teaching is set forth, either by the use of illustrative examples or by broad terminology, is of no importance." *In re Marzocchi*, 169 USPQ 367 , 369 (CCPA 1971).

Thus, the use of broad terminology does not mean a claim is not properly enabled. In the present instance, a person of skill in the art would be able to use the preparation set forth in claim 14. Accordingly, claim 14 is properly enabled.

The court also added that "it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of

any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure." *In re Marzocchi*, 169 USPQ 367 , 370 (CCPA 1971). The present record does not adequately explain why the truth of the accuracy of statements in the disclosure should be doubted.

The stated reasons for the rejection fall outside the test for enablement articulated by the court in *In re Marzocchi*. These reasons clearly do not provide any explanation as to why the objective assertions by the applicants in the disclosure should be doubted.

Thus, persons of skill in the art could practice the claimed invention and would reasonably expect that the claimed methods of detecting pain-regulating substances with PIM-kinases would be operative. Reconsideration and withdrawal of this rejection are therefore respectfully requested.

The rejection of claims 1 – 15, 32 – 34 and 47 under 35 U.S.C. 102(b) as being anticipated by Koike et al. (FEBS Letters, Vol. 467, pp. 17 – 21, 2000) as evidenced by Bachmann et al. (The International Journal of Biochemistry & Cell Biology, Vol. 37, pp. 726 – 730, 2005) is respectfully traversed.

Claims 1 – 15 and 32-34 relate to the discovery that certain PIM-kinases have relevance to pain states. In particular, claim 1 recites a method for detecting a pain-regulating substance and each of claims 1-15 and 32-34 are dependent therefrom. Accordingly all of these claims are directed to a method for detecting a pain-regulating substance.

Koike et al. suggests that *pim*-1 may have relevance to chromatin dynamics, see page 20. This relevance is suggested to be affected by phosphorylation of heterochromatin protein 1γ. The reference does not disclose the claimed method of detecting a pain-regulating substance or even that certain PIM-kinases have

relevance to pain states. Accordingly, there is no way a person of skill in the art could take the teachings of Koike and practice the claimed method.

Claim 47 relates to a method for investigating the activity of a test substance with a step that involves incubating a test substance with the active ingredient of claim 36.

Koike fails to teach incubating with a test substance as is presently contemplated by claim 47. To qualify as a test substance, the properties of the test substance (in particular whether it will bind the active ingredient of claim 36 or otherwise interact with the active ingredient so as to modify a functional parameter) must be unknown. Thus, the method allows one to determine whether the test substance has some relevance to the active ingredient of claim 36, as evidenced by the binding or other modification resulting from the interaction thereof.

The Office Action asserts that sections 2.2, 2.3 and 2.5 of Koike are relevant. Section 2.2 of Koike simply provides names for various constructs used in the experiments. Section 2.3 discloses transforming cells with one of these constructs and then transforming again with HeLa MATCHMAKER cDNA and screening for lacZ expression. There is no test substance in this method as the transformed cells are simply screened to verify the transformation. Nothing is learned about any test substance, rather all that is learned is whether transformation was successful. Section 2.5 discloses a binding assay where a partial Pim-1 construct was transfected to cells and cell extracts were immunoprecipitated and analyzed. While this method shows binding of the partial Pim-1 construct to heterochromatin protein 1γ, the method does not appear to anticipate the claimed invention which requires an active ingredient which is defined by categories a-h of claim 36.

The Federal Circuit has held that lack of novelty (anticipation) under 35 U.S.C. § 102 requires, among other things, identity of invention. *Minnesota Min. & Mfg. Co. v. Johnson & Johnson Orthopaedics, Inc.*, 976 F.2d 1559, 24 USPQ2d 1321

(Fed. Cir. 1992). Further, anticipation requires that each and every element of the claimed invention be disclosed in a single prior art reference or embodied in a single prior art device or practice. *See, e.g., Bristol-Myers Squibb Co. v. Ben Venue Laboratories, Inc.*, 58 USPQ2d 1508, 1512 (Fed. Cir. 2001), *reh'g and reh'g en banc. denied,* (Fed. Cir. 2001). As explained above, the Koike reference fails to teach all of the elements of the presently claimed invention. Accordingly, the anticipation rejection cannot be properly maintained. Reconsideration and withdrawal of the rejection are therefore respectfully requested.

The rejection of claims 1 – 3, 5 – 7, 9 – 15, 32 – 34 and 47 under 35 U.S.C. 102(e) as being anticipated by Reinhard et al. (U.S. Patent Application Publication No. 2003/0045491) is respectfully traversed.

These claims are described immediately above.

Reinhard et al. is directed to disease diagnosis and treatment of cancer and identification of anti-cancer agents, see paragraph [0002] of the disclosure. The Office cites paragraphs [0119-0122] as teaching screening assays to identify proteins or other substrates that bind to or modulate the action of certain proteins. None of these paragraphs disclose the claimed method of detecting a pain-regulating substance or even that certain PIM-kinases have relevance to pain states. Accordingly, Reinhard et al. does not disclose the inventive method of claims 1-3, 5-7, 9-15 and 32-34.

Moreover, the Office Action relies on certain sequences provided in Reinhard et al. and asserts that Reinhard teaches the TTK proteins "such as PIM-1." However the nucleotide sequences relied on for this assertion that these TTK proteins are so similar (the assertion appears to be that they are the same as) PIM-1 proteins are not disclosed in the provisional application from which Reinhard claims the benefit (U.S. Application No. 60/289,813 filed February 21, 2001). The text of the disclosure of both the provisional application and Reinhard 2003/0045491

both indicate that TTK and PIM-1 are related kinases, but not that they are the same (see paragraph [0004] of the published application and on page 1 of the provisional application). The disclosure of the provisional application does not appear to indicate anywhere that PIM-1 might be a suitable substitute for TTK. Other than the mention of PIM-1 as a related kinase, the provisional application does not appear to even suggest that the methods taught therein might be applicable to PIM-1. As a result, the provisional application fails to support the disclosure of the published application, at least as far as the published application is deemed to disclose "TTK polynucleotides encoding TTK proteins such as PIM-1" as suggested in the recent Office Action. These polynucleotides sequences do not appear to have been provided in the provisional. Instead, the provisional discloses a variety of different oligonucleotides. As a result, the published application is limited to its filing date of February 21, 2002 for the subject matter of the sequences relied on in the Office Action.

The present application claims priority to DE 10123055.9 which was filed May 11, 2001. A certified copy of this application has been made of record. According, the present application is entitled to the benefit of the filing date of the German application, thereby predating and removing the reference for these purposes.

Reconsideration and withdrawal of the rejection are respectfully requested.

CONCLUSION

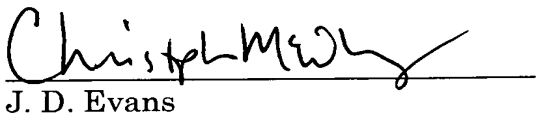
In view of the foregoing, the application is respectfully submitted to be in condition for allowance, and prompt favorable action thereon is earnestly solicited.

If there are any questions regarding this amendment or the application in general, a telephone call to the undersigned would be appreciated since this should expedite the prosecution of the application for all concerned.

Although an Extension of Time is submitted herewith, if necessary to effect a timely response, this paper should be considered as a petition for an Extension of Time sufficient to effect a timely response, and please charge any deficiency in fees or credit any overpayments to Deposit Account No. 05-1323 (Docket #029310.52818US).

Respectfully submitted,

March 29, 2006



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